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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/619,715	07/14/2003	Oleg Chertov	14014.0383U3	7997

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EXAMINER	
CROWDER, CHUN	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/619,715	CHERTOV ET AL.	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) and 120 is acknowledged. The priority applications upon which benefit is claimed appears to provide adequate support under 35 U.S.C. 112 for subject matter claimed in the instant application.

2. If applicant desires benefit of a previously filed application under 35 U.S.C. 119(e), specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence(s) of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

3. The specification on page 1, line 2 should be amended to reflect the status of the parent application USSN 09/960,876 which is now abandoned.

4. Applicant's IDSs, filed October 3, 2003 and May 27, 2005, are acknowledged, and have been considered.

5. *Claims* 1-7 *are under consideration in the instant application.*

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 are indefinite in the recitation of "LL-37" because there are not sufficient characteristics to clearly define the structure of this peptide. It is suggested that the amino acid sequence of LL-37 be recited in the claims.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

9. The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be

accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. *In re Hawkins*, 486 F.2d 569 179 USPQ 157 (CCPA 1973); *In re Hawkin*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); *In re Hawkins*, 486 F2.d 577, 179 USPQ 167 (CCPA 1973).

10. The attempt to incorporate LL-37 into this application by reference to Gudmundsson *et al* (Eur. J. Biochem. 1996; 238: 325-332) disclosed on page 2, lines 3-4 of the specification is improper because essential material can not be incorporated by reference to a publication. Applicant is required to amend the specification to disclose the amino acid sequence of LL-37 published in the Gudmundsson *et al* (Eur. J. Biochem. 1996; 238: 325-332). The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. *In re Hawkins*, 486 F.2d 569 179 USPQ 157 (CCPA 1973); *In re Hawkin*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); *In re Hawkins*, 486 F2.d 577, 179 USPQ 167 (CCPA 1973).

For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1-4 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,440,690, as is evidenced by Gudmundsson *et al*, (Eur. J. Biochem. 1996; 238: 325-332) (1449; #A15) and the known fact disclosed on pages 1-2 of the instant application.

The '690 Patent teaches a method of activating host immune system by administrating a human cationic antimicrobial peptide FALL-39/CAP-18 to a human or non-human animal (see column 28, last paragraph and column 1, lines 14-16 in particular). The '690 Patent further teaches this cationic antimicrobial peptide as having a stimulatory effect on the host immune system by activating cells of the monocyte/ macrophage lineage and/or other lymphoid cells (see column 2, lines 55-61 in particular). As is evidenced by the specification disclosure on pages 1-2 and by Gudmundsson *et al* (Eur. J. Biochem. 1996; 238: 325-332) that human FALL-39/CAP-18 is LL-37. Given the use of the identical FALL-39/CAP-18/LL-37 cathelicidin to enhance an immune response by activating lymphocytes in a mammal including a human, there does not appear to be a manipulative difference between the prior art methods and the claimed methods of enhancing immune responses, including adaptive immune responses by administering LL-37.

Although the reference is silent about the enhancing an adaptive immune response per se, it does not appear that the claim limitation results in a manipulative difference in the methods steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d1508 (CAFC2001). It is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable.

Thus the reference teachings anticipate the claimed invention.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tani *et al* (Int Immunol. 2000 May;12(5):691-700) in view of Nagaoka *et al* (Inflamm. Res. 2000 Feb.; (49): 073-079) and US Patent No. 6,440,690. As is evidenced by Gudmundsson *et al*, (Eur. J. Biochem. 1996; 238: 325-332) (1449; #A15) and the known fact disclosed on pages 1-2 of the instant application.

Tani *et al* teach that antimicrobial peptide defensins act as potent adjuvants that enhance host immune response in mice. Further, when combined with syngeneic tumor antigen, defensins significantly prolonged survival in mice inoculated with lymphoma (see page 691, abstract and page 695, right column in particular).

The claimed invention differs from the reference teachings only by the recitation of antimicrobial peptide LL-37 in combination with a vaccine to enhance immune response.

Nagaoka *et al* teach that defensins and CAP/LL-37 have synergistic actions under physiological condition (see page 74, first paragraph of the left column in particular).

The '690 Patent teaches that cationic antimicrobial peptides including FALL-39/CAP-18 can activate host immune system by activating monocyte/macrophage lineage and/or other lymphoid cells in human or non-human animal (see column 28, last paragraph and column 1 lines 14-16 in particular). As is evidenced by Gudmundsson *et al*, (Eur. J. Biochem. 1996; 238: 325-332) (1449; #A15) and the known fact disclosed on pages 1-2 of the instant application, that LL-37 is LL-37/hCAP-18.

Therefore, it would have been obvious to one of the ordinary skill in the art at the time the invention was made to include LL-37 taught by the '690 Patent in the method of enhancing immune response to a vaccine using defensins as taught by Tani *et al* to achieve a synergistic action as taught by Nagaoka *et al*. The word "comprising" is open-ended; it would open up the claim to include the defensins in the method of enhancing immune response to a vaccine.

One of ordinary skill in the art at the time the invention was made would have been motivated to utilize LL-37 taught by the '690 Patent in combination with a vaccine to enhance the immune response as taught by Tani *et al*. Given that Nagaoka *et al* teach that defensins and LL-37 work synergistically and LL-37 can activate monocyte/macrophages and lymphocytes as taught by the '690 Patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in arriving

at the claimed invention. Therefore, the claimed invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tani *et al* (Int Immunol. 2000 May;12(5):691-700) in view of the '690 Patent, as is evidenced by Gudmundsson *et al* (Eur. J. Biochem. 1996; 238: 325-332) and the known fact disclosed on pages 1-2 of the instant application.

The Tani *et al* reference has been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of antimicrobial peptide LL-37 in combination with a vaccine to enhance immune response.

The '690 Patent teaches that cationic antimicrobial peptides including FALL-39/CAP-18 can activate host immune system by activating monocyte/macrophage lineage and/or other lymphoid cells in human or non-human animal (see column 28, last paragraph and column 1 lines 14-16 in particular). As is evidenced by Gudmundsson *et al*, (Eur. J. Biochem. 1996; 238: 325-332) (1449; #A15) and the known fact disclosed on pages 1-2 of the instant application, that LL-37 is LL-37/hCAP-18.

Therefore, it would have been obvious to one of the ordinary skill in the art at the time the invention was made to substitute cationic antimicrobial peptide defensins taught by Tani *et al* reference with another cationic antimicrobial peptide LL-37 taught by the '690 Patent to enhance an immune response to a vaccine.

One of ordinary skill in the art would have been motivated to do so, because Tani *et al* teach that antimicrobial peptide defensins are potent adjuvants that enhance host immune response and the '690 Patent teaches that cationic antimicrobial peptides

including FALL-39/CAP-18 activate host immune system by activating monocyte/macrophage lineage and/or other lymphoid cells.

From the teachings of the references, it was apparent that on of ordinary skill in the art would have a reasonable expectation of success in arriving at the claimed invention. Therefore, the invention as a whole was prima facie obvious to on of ordinary skill in the art at the time the invention was made, as evidenced by references, especially in the absence of evidence to the contrary.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.
Patent Examiner
June 27, 2005

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